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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,775	11/02/2001	Gordon Freeman	GNN-004ADV	6215

959 7590 06/29/2004

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,775	FREEMAN ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of this application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Ilia Ouspenski, Group Art Unit 1644, Technology Center 1600.

2. Applicant's preliminary amendments, filed 11/02/2001 and 02/20/2002, are acknowledged and have been entered.

Claims 1 – 11 and 17 – 24 have been cancelled.
Claims 12 – 16 are pending.

Claims 12 – 16 are under consideration in the instant application.

3. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Provisional application 60/150,390 appears to provide adequate written support for the instant claims drawn to SEQ ID NOS:2 and 4, human B7-4 molecules.

5. Applicant's IDS, filed 04/12/2002, is acknowledged.

6. Preliminary Amendment, filed 11/02/2001, is acknowledged and has been entered.

The Amendment is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "[] application serial number 09/644,934 [is] incorporated herein in [its] entirety by this reference."

Applicant is required to cancel the new matter in the reply to this Office action.

See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003): "An incorporation-by-reference statement added after the filing date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 USC §132(a). If an incorporation-by reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include incorporation-by-reference statement of the prior application. See Dart Industries v. Banner, 636 F.2d 684, 207 USPQ 273 (C.A.D.C. 1980). Therefore, the Office will not grant a petition to accept a benefit claim that includes an incorporation-by-reference statement of a prior application, unless the incorporation-by-reference statement was submitted on filing of the application."

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

In addition, Applicant should avoid the use of the word "novel" in the title, as patents are presumed to be novel and unobvious.

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at least on page 10, line 19. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Applicant is requested to review the application for embedded hyperlinks and/or other forms of browser-executable code and delete them. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. See MPEP § 608.01 and 608.01(p).

The use of the trademarks, for example Triton® X-100 (page 74, line 11), has been noted in this application. Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

9. Claim 16 is objected to because of the following informalities: it appears that "amino acids 19 – 245 or SEQ ID NO:2" was intended to read "amino acids 19 – 245 of SEQ ID NO:2." Appropriate correction is required.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 12 – 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12, and dependent claims thereof, are ambiguous in reciting "stringent conditions." Although the specification discloses on page 21 at lines 14 – 17 that "stringent conditions" include particular parameters in a non-limiting example, in the absence of a definition that clearly provides the metes and bounds of this phrase, it is unclear which conditions are actually claimed.

It is suggested the applicant amend the claims to recite the hybridization and wash conditions disclosed on page 21 at lines 14 – 17 of the specification to overcome this rejection.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 12 - 16 are rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

Claim 12 recites fragments of SEQ ID NOS:2 or 4, allelic variants, and polypeptides encoded nucleic acids which hybridize or are homologous to SEQ ID NOS: 1 or 3.

The essential element of the invention is considered to be the structural and functional characteristics shared by the disclosed polypeptides of SEQ ID NOS:2 and 4, respectively, wherein the polypeptides costimulate proliferation of activated T cell, as disclosed in the Specification on page 99 at lines 20-21.

Claim 12(a) recites various fragments of SEQ ID NOS:2 or 4. Further, the language of claim 12(b) appears to encompass fragments, in recitation of the hybridization language. Even under high stringency conditions, molecules shorter than the specified sequence are expected to meet this limitation. However, Applicant does not appear to have identified which fragments of any particular length or over a particular region are essential for the function of the polypeptides of SEQ ID NOS:2 or 4. Neither does the specification appear to have provided any working examples of any functional subsequences. Thus it would require undue experimentation of the skilled artisan to determine which fragments of SEQ ID NOS:2 or 4 would have the function of the full length molecule.

Recitation of the term "allelic variant" in claim 12(b) encompasses a large genus of nucleic acids, since an "allele" is any one of a series of two or more different genes that may occupy the same position or locus on a specific chromosome (Stedman's Medical Dictionary, 24th Edition, 1982 Williams & Wilkins, Baltimore MD; IDS # A9). Applicant does not appear to have provided a representative number of species of allelic variants, nor to have provided a description of mutational sites that exist in SEQ ID NOS:1 or 3. The common attributes of this genus do not appear to have been described, nor has Applicant set forth the identifying attributes of individual alleles other than SEQ ID NO:1 or 3. Finally, the instant claims do not provide a functional characteristic(s) that identifies members of the genus of allelic variants of SEQ ID NOS:1 or 3.

The additional limitation that the allelic variant be encoded by a nucleic acid which hybridizes under stringent conditions to SEQ ID NOS:1 or 3 still encompasses an extensive genus of nucleic acids. Furthermore, the specification does not define the degree of complementarity that is encompassed by the claim's hybridization language. The specification on page 21 at lines 7-12 teaches that "under stringent conditions" encompasses molecules which are from 30% to 90% identical to SEQ ID NOS:1 or 3. Thus the hybridization language itself also encompasses a large number of nucleic acids, many of which would bear little resemblance to the B7-4 nucleic acid sequence of the claimed invention. Consequently, Applicant does not appear to be in possession of the claimed genus of "allelic variants".

Similarly, in recitation of percent identity language (claim 12(c) and (d)), Applicant does not appear to have established which residues within either the full length sequence or the fragments can be changed and still maintain a correlative function shared by a genus of nucleic acids having at least 50% identity to SEQ ID NOS: 1 or 3 or hybridizing to these sequences under stringent conditions. The level of variation within both the genus of molecules with 50% identity is high.

Further, instant claim 12(b – d), in the absence of a limitation requiring that the homology or hybridization occur over the full length of the molecule, combines the variables of a fragment and a homologous/hybridizing molecule, permitting extensive variation among members of the genus. Thus the skilled artisan would reasonably conclude that the disclosure fails to provide a representative number of species to describe the highly variable genus of nucleic acid molecules encompassed by claim 12, and dependent claims thereof.

Applicant has disclosed only polypeptides SEQ ID NOS:2 and 4, and nucleic acids of SEQ ID NOS:1 and 3; therefore, the skilled artisan cannot

envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993).

The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

14. Claims 12 – 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS:2 and 4, does not reasonably provide enablement for the various polypeptides comprising fragments, allelic variants encoded by nucleic acids which hybridize with disclosed sequences, or polypeptides which are at least 50% identical, or are encoded by nucleic acids which are at least 50% identical, to disclosed sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification does not provide a sufficient enabling description of the claimed invention. A person of skill in the art is not enabled to make and use these many nucleic acid sequence variants as recited in the instant claims.

Applicant does not appear to have identified which polypeptide fragments are essential to the function of a B7-4 protein. Thus it would be unpredictable which, if any, contiguous 15 amino acids of the polypeptide encompassed the functional activity of a B7-4 protein. It is further noted that a "fragment comprising" undisclosed sequences encompasses a myriad of sequences, few if any of which would be expected to share functionality with the instant B7-4 sequences. In view of this uncertainty, it would be even more unpredictable as to which other "fragments" having less than 100% identity would still maintain the costimulatory function of the B7-4 polypeptides.

Further, there does not appear to be sufficient guidance for the skilled artisan to make and use "allelic variant" nucleic acids. As noted supra, the term "allelic variants" encompasses any one of a series of two or more different genes that may occupy the same position or locus on a specific chromosome (Stedman's Medical Dictionary, 24th Edition 1982 Williams & Wilkins, Baltimore, MD; IDS # A9). However, allelic variants do not necessarily encode proteins having the same function. For exemple, Voet et al. (In Biochemistry, John Wiley & Sons. 1990, Vol. 1, pages 126-128, and page 230; IDS # A10) teaches that a single Glu to Val substitution in the β subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals (i.e., those in which both alleles encode the sickle-cell variant), erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-127 and page 230, paragraph bridging columns in particular). Thus allelic variants can encode proteins having drastically different functions, even when the proteins share a high level of sequence and structural homology. However, the term "allelic variant" only requires that the same locus be occupied; thus not only are the changes in function to similar base sequences unpredictable; but the term does not actually require any conservation of function. Even with the limitation of being encoded by a nucleic acid which hybridizes to SEQ ID NO: 1 or 4, it would require undue experimentation of the skilled artisan to identify nucleic acids that are "allelic variants" of SEQ ID NOS:2 and 4 and determine which of those proteins having the same function as the instant B7-4 polypeptides.

As set forth supra, the skilled artisan also lacks sufficient guidance with respect to how to make nucleic acid molecules which "hybridize under stringent conditions" as currently recited. Even were hybridization parameters clearly recited, in the absence of language reciting a function shared by the hybridizing nucleic acids, such as encoding proteins which costimulate proliferation of activated T cells, the experimentation left to one skilled in the art would still be extensive and undue since hybridizing nucleic acids would not necessarily share the same functional properties as the instant B7-4 sequences.

Similarly, there appears to be insufficient guidance in the specification as-fled to direct a person of skill in the art to select particular sequences as essential for the functional properties of a polypeptide comprising a sequence that has "at least 50% identity" to the polypeptide of SEQ ID NO:2 or 4, or encoded by a nucleic acid which has "at least 50% identity" to the nucleotide sequence of SEQ ID NOS: 1 or 3 as recited in the instant claims. Attwood (Science 29045491):47 1-473, Oct. 27, 2000; IDS # A2) teaches in her Introductory paragraphs that it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences (and it is not always clear what we mean by "function"); very few structures are known compared with the number of sequences, and structure prediction methods are unreliable (and knowing structure does not inherently tell us functions) [parentheses added]. Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000; IDS # A8) teach that even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the skilled artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). This requirement is emphasized in the instant example since, as summarized in Figures 2 and 3 of Coyle et al. (Nature Immunol. 2:203-209 2001; IDS # A3) the B7-like family members have distinct expression patterns *and distinct functions*. Thus the experimentation left to those skilled in the art to determine the function of proteins having at least 50% identity, or encoded by

nucleic acids having at least 50% identity, is unnecessarily, and improperly, extensive and undue.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the experimentation left to those skilled in the art to determine which sequence fragments, homologous sequences, or hybridizing sequences would still maintain the function of SEQ ID NOS:2 and 4 is unnecessarily, and improperly, extensive and undue.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claim 12 is rejected under U.S.C. 102(b) as being anticipated by GenBank entry Accession #AA292201 (IDS #A11, see entire document).

GenBank Accession #AA292201 from about residues 9-497 is identical to instant SEQ ID NO:1 from about residues 320-807 (see attached alignment). In addition, #AA.292201 from about residues 9-430 is identical instant SEQ ID NO:3 from about residue 315-734. Thus AA292201 meets the limitation of a nucleic acid molecule which encodes a 15 amino acid contiguous fragment of SEQ ID NOS:2 or 4. Likewise, #AA292201 encodes a polypeptide is at least about 50% identical to the amino acid sequence of either SEQ ID NO:2 or 4, or which is encoded by a nucleic acid which is at least 50% identical to SEQ ID NO:1. or 3, since no limitation requiring the identity to be over the full length of the polypeptide is recited. Given the 100% identity over a long region of sequence, AA292201 would also hybridize to nucleic acids comprising SEQ ID NOS: 1 or 3, which would encode allelic variants of polypeptides SEQ ID NOS:2 or 4.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of GenBank Accession #AA292201.

Thus the teachings of the reference anticipate the instant invention.

Conclusion

17. No claim is allowed.

Claims 13 – 16 appear to be free of prior art.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

June 21, 2004

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
6/23/04